nature portfolio

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data was collected with the OracleInForm Electronic Data Capture (v7.0)
Data analysis	Data was analyzed using R Software (v.4.4.1). Analyses were performed in R using the packages tidyverse (v2.0.0), ggplot2 (v4.0.2), dplyr (v1.1.4), tidyr (v1.3.1), readr (v2.1.5), readxl (v1.4.3), stringr (v1.5.1), purrr (v1.0.2), forcats (v1.0.0), lubridate (v1.9.3), lme4 (v1.1-35.5), lmerTest (v3.1-3), survival (v3.7-0), survminer (v0.4.9), prodlim (v2024.06.25), ggpubr (v0.6.0), ggtext (v0.1.2) and pracma (v2.4.6), splines (v.4.4.1). No custom code or mathematical algorithm was specifically developed for this study.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The data supporting the findings of this study are derived from an ongoing clinical trial and are not publicly available. Qualified researchers may submit requests for

de-identified participant data to the corresponding author, together with a description of the specific data requested, the proposed analyses and the dissemination plan. Requests will be reviewed by the study lead and the trial sponsor, and data may be shared upon publication following review and execution of a data-sharing agreement, subject to participant confidentiality and applicable regulatory requirements. Responses to data requests are typically provided within 3 months. A redacted trial protocol including the statistical analysis plan are available in the Supplement.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	This study enrolled adult human participants with high-risk smoldering multiple myeloma. Sex was recorded from the clinical record. Gender was not analyzed separately because gender-related data were not collected in a standardized manner relevant to the study objectives. Sex was considered as a baseline demographic characteristic but was not used to stratify analyses because of the small sample size and the early-phase, safety-focused design.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity were recorded from the clinical record and/or self-report, where available, as part of routine clinical documentation. These variables were collected for descriptive reporting of the study population. Given the small cohort size, the single-center design, and limited statistical power, analyses stratified by race or ethnicity were not performed.
Population characteristics	The study population consisted of adult participants with high-risk smoldering multiple myeloma enrolled at a single academic center. Covariate-relevant characteristics included age, sex, race and ethnicity where available, disease-specific risk features, bone marrow plasma cell burden, laboratory parameters, cytogenetic risk features, prior disease history, and treatment-related variables relevant to study eligibility and outcome assessment. Participants were treatment-naive for myeloma-directed systemic therapy in the smoldering setting and met prospectively defined eligibility criteria as described in the protocol and Methods.
Recruitment	Participants were recruited at Dana-Farber Cancer Institute from patients evaluated for eligibility for this single-center clinical trial in high-risk smoldering multiple myeloma. Enrollment was based on predefined protocol eligibility criteria and written informed consent was obtained from all participants before study procedures. Because this was a single-center early-phase trial, potential sources of bias include referral bias, volunteer/self-selection bias among patients willing to participate in a clinical trial, and selection bias introduced by protocol eligibility criteria.
Ethics oversight	The study protocol was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board. The trial was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All participants provided written informed consent before study participation.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample size was determined by the study design rather than to power a formal hypothesis test for the primary endpoint. This was a phase 2 study primarily designed to evaluate safety and feasibility. The planned sample size also incorporated a prespecified single-stage exact binomial design for the complete response endpoint, under which a complete response rate of 40% was considered promising and 5% not promising; with 20 treated patients, the study would be considered positive if at least 4 complete responses were observed.
Data exclusions	No participants were excluded from the analyses after treatment initiation. For longitudinal correlative and laboratory analyses, missing data were not imputed, and analyses at each time point were based on available samples and evaluable measurements.
Replication	Clinical, laboratory, and correlative assessments were performed according to the protocol and prespecified assay procedures. Clinical endpoints were assessed across all treated participants in the cohort.
Randomization	This was a single-arm, non-randomized clinical trial.
Blinding	Blinding was not used in this study because this was a single-arm clinical trial without randomized group assignment.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

BCMA CAR Detection Reagent, human — FITC — Miltenyi
CD16 — APC — clone 3G8 — BioLegend
PD-1 — PE-Cy7 — clone J105 — Invitrogen
CD19 — BV711 — clone HIB19 — BioLegend
CD45 — APC-Cy7 — clone 2D1 — BD Biosciences
CD8 — Alexa Fluor 700 — clone RPA-T8 — BioLegend
CD278 (ICOS) — BV421 — clone C398.4A — BioLegend
CD3 — BV786 — clone UCHT1 — BioLegend
CD4 — BV510 — clone RPA-T4 — BioLegend
CD56 — BV605 — clone NCAM — BioLegend
CD14 — BV650 — clone M5E2 — BioLegend
CD137 (4-1BB) — PE — clone 4B4-1 — BioLegend
7-AAD (viability) — PE-Cy5 / PerCP-Cy5.5 — BD Biosciences
CD45RO — APC — clone UCHL1 — BD Biosciences
CD127 — PE — clone A019D5 — BioLegend
CD95 — BV421 — clone DX2 — BioLegend
CD25 — BV605 — clone M-A251 — BioLegend
CD161 — BV650 — clone DX12 — BD Biosciences
CCR7 — BV711 — clone G043-H7 — BioLegend

Validation

Antibodies were used in accordance with manufacturer validation and established flow cytometry practice. Staining conditions were optimized using standard assay controls.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration

This study is registered at ClinicalTrials.gov under identifier NCT05767359

Study protocol

A redacted study protocol is provided with the Supplementary Information.

Data collection

Data were collected at Dana-Farber Cancer Institute as part of a single-center phase 2 clinical trial in patients with high-risk smoldering multiple myeloma. Participants were recruited and enrolled between 4/15/2023 and 7/3/2025. Clinical, laboratory, and correlative data were collected prospectively at protocol-defined study visits from screening through treatment and follow-up, including baseline, leukapheresis, lymphodepletion, infusion, and post-infusion follow-up assessments. Data collection continued through the study data cutoff on 2/11/2026.

Outcomes

The primary outcome was safety, assessed by the incidence of dose-limiting toxicities within the prespecified post-infusion assessment window, together with adverse event monitoring throughout follow-up. Adverse events, including cytokine release syndrome and neurologic toxicities, were assessed clinically and graded according to protocol-specified criteria. Secondary outcomes included feasibility/manufacturing success, response, complete response rate, minimal residual disease negativity, progression-free survival, duration of response, pharmacokinetics, pharmacodynamic biomarkers, and immunogenicity. Response outcomes were assessed using protocol-defined clinical, laboratory, bone marrow, and minimal residual disease evaluations, and time-to-event outcomes were assessed from protocol-defined start points as described in the Methods.

Plants

Seed stocks — *Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes — *Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication — *Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation — Peripheral blood and/or bone marrow mononuclear cells obtained from study participants were processed using standard laboratory procedures and stained with antibody panels for flow cytometric analysis. Sample handling, viability assessment, and staining were performed according to established protocols.

Instrument — Fortessa LSR (BD Biosciences)

Software — FACSDiva and FlowJo v10

Cell population abundance — Not applicable. Cells were not physically sorted before analysis. Flow cytometry was performed on bulk peripheral blood mononuclear cell samples, and cell populations were identified analytically by sequential gating rather than post-sort purification.

Gating strategy — Cells were gated sequentially to exclude debris, doublets, and dead cells, followed by identification of relevant immune cell populations on the basis of marker expression; representative gating is shown in the Supplementary Information.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.